CASE REPORT

Fulminant eosinophilic endomyocarditis in an asthmatic patient treated with pranlukast after corticosteroid withdrawal

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Abstract

Several cases of eosinophilic conditions including Churg-Strauss syndrome have been reported in association with the use of cysteinyl leukotriene receptor antagonists, including zafirlukast, montelukast, and pranlukast, in asthmatic patients. The case of a 26 year old woman with a three year history of asthma, rhinitis, and nasal polyps is reported in whom eosinophilia, pulmonary infiltrates, and fulminant eosinophilic endomyocarditis accompanied by cardiogenic shock developed during pranlukast treatment after corticosteroid withdrawal. Acute necrotising eosinophilic endomyocarditis was confirmed by endomyocardial biopsy. The patient recovered after intensive treatment, including mechanical assistance involving intra-aortic balloon pumping and steroid pulse therapy, along with the discontinuation of pranlukast. It is recommended that careful attention must be paid to signs of a systemic eosinophilic condition or even fulminant eosinophilic myocarditis in asthmatic patients who have begun treatment with antileukotriene drugs following withdrawal of steroids.

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Keywords: fulminant eosinophilic endomyocarditis; asthma; pranlukast

In 1998, Wechsler and colleagues¹ described the cases of eight asthmatic patients taking zafirlukast, a cysteinyl leukotriene receptor antagonist (LTRA), who developed Churg-Strauss syndrome after corticosteroid withdrawal. Since then, similar cases have been reported among asthmatics who were taking two other LTRAs, montelukast and pranlukast.²⁻³ To our knowledge, this is the first report of an asthmatic patient in whom a systemic eosinophilic syndrome accompanied by life threatening cardiac involvement developed during the use of pranlukast treatment after corticosteroid withdrawal.

Case report

A 26 year old woman was transferred to our hospital in September 2000 because of eosinophilia, cardiogenic shock, and pulmonary

infiltrates. She had a three year history of persistent asthma, perennial rhinitis, and nasal polyps. Her asthma had been managed with 5 mg/day oral prednisolone, 200 mg/day theophylline, and 800 µg/day inhaled beclomethasone. During that time her eosinophils had ranged from 2–8% and chest radiograph findings were normal. The oral prednisolone was discontinued and replaced by pranlukast in December 1999, and the inhaled beclomethasone was continued. Three weeks before admission, the patient developed slight fever, malaise, and coughing. During the subsequent weeks, her coughing got worse and she developed breathlessness. On admission, she was severely exhausted and orthopnoeic. Her temperature was 37.1°C, blood pressure 75/45 mm Hg, pulse 130 beats/min and regular, and respiration 30 breaths/min. Crackles were heard in both lung fields, and the cardiac sound was indistinct, but neither skin lesions nor neurological abnormalities were found. Laboratory studies indicated a white blood cell count of $11.5 \times 10^9/l$ with 29% ($3.3 \times 10^9/l$) eosinophils, an erythrocyte sedimentation rate of 92 mm/h, and 150 mg/l of C-reactive protein. Serum eosinophilic cationic protein (51 µg/l; normal < 15.7 µg/l) was increased. Creatine kinase was increased to 372 U/l with a notable creatine kinase MB fraction concentration of 27 U/l (7.3%). Serum immunoglobulin E was normal, and antineutrophil cytoplasmic antibodies were negative. No parasitic eggs were found in the stool. Chest radiograph and computed tomography showed cardiomegaly and bilateral opacities (fig 1). An ECG showed sinus tachycardia, poor R wave progression, and ST elevation in leads V1–4. Echocardiography showed diffuse severe left ventricular hypokinesia with an ejection fraction of 19% and a small pericardial effusion. Coronary arteriographic examination results were normal.

Endomyocardial biopsy from the right ventricle indicated acute necrotising eosinophilic endomyocarditis (figs 2A,B). Immunostaining with a monoclonal antibody (EG2), specific to activated eosinophils and binding to the secreted forms of eosinophilic cationic protein and eosinophil protein X,⁴ showed the presence of many activated eosinophils and dense deposits of eosinophilic cationic protein and eosinophil protein X in the endocardium (fig

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Figure 1 Chest radiograph (A) and computed tomographic scan (B) on admission. Cardiomegaly and bilateral opacities can be seen.

2C) as well as the myocardium (fig 2D). Neither granuloma nor vasculitis was detected.

Pranlukast use was stopped, and after intensive treatment, including catecholamine infusion, intra-aortic balloon pumping, and steroid pulse therapy for four days followed by 60 mg of prednisolone, the patient's haemodynamic status improved with a rapid decrease in the eosinophil count and serum eosinophilic cationic protein concentration. The patient was weaned from the intra-aortic balloon pumping and catecholamine injections on the ninth and 12th hospital day, respectively. Subsequent echocardiography showed an increase in left ventricular systolic function with ejection fraction of 40%, although regional wall thinning and hypokinesis were evident in the midinterventricular septum. Repeated right endomyocardial biopsy performed on the 58th hospital day showed a disappearance of eosinophils and acute inflammation, but endocardial and interstitial fibrosis had developed. The prednisolone dose was gradually tapered off to 10 mg/day without further disease flare-up.

Discussion

The clinical association between Churg-Strauss syndrome and the use of LTRAs has recently generated widespread interest.⁵ Although it is possible that LTRAs can directly cause Churg-Strauss syndrome,⁶ most reports have suggested that the introduction of LTRAs allows for steroid dose reduction, thereby unmasking an underlying forme fruste of this syndrome.^{1,7} Our patient met the criteria of

Figure 2 Right ventricular endomyocardial biopsy obtained on the day of admission. Haematoxylin and eosin staining shows severe eosinophilic infiltration to the endocardium (A) and myocardium (B) in association with cardiac myocyte necrosis. Immunostaining with EG2, a monoclonal antibody against the eosinophilic cationic protein, shows the presence of many activated eosinophils and dense deposits of eosinophilic cationic protein in the cardiac tissue (C and D). Bar = 50 μ m.

Churg-Strauss syndrome⁸ but lacked several common manifestations of Churg-Strauss syndrome such as mononeuritis multiplex or skin lesions. This atypical presentation of Churg-Strauss syndrome suggests that the patient might have developed a Churg-Strauss syndrome like illness caused by the leukotriene inhibitor pranlukast.⁹

Wechsler and colleagues¹ suggested cardiac manifestations to be more frequent in patients with Churg-Strauss syndrome treated with LTRAs than in those not given LTRAs. There have been no prior reports, however, of fulminant eosinophilic myocarditis associated with LTRA treatment of such severity that a mechanical circulatory assistance device was required. Our experience with this patient suggests that physicians should be aware that LTRAs may cause Churg-Strauss syndrome or even fulminant eosinophilic myocarditis following steroid withdrawal.

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